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Faster . . . but Fast Enough?

Responding to the Epidemic of Severe Acute Respiratory Syndrome

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Severe acute respiratory syndrome (SARS) was diagnosed in more than 1800 patients in 17 countries (including the United States and Canada) between February 1 and March 31, 2003. During this two-month period, the World Health Organization (WHO) coordinated an international investigation that has produced unprecedented scientific and epidemiologic discoveries with unprecedented speed. On March 12, the WHO issued a global alert about SARS. On March 14, the Centers for Disease Control and Prevention (CDC) activated its emergency operations center to support the response of the WHO to this global threat. Within 24 hours of the official invitations, CDC investigators joined WHO field teams in several affected Asian countries, supported by the full complement of laboratory, epidemiologic, communications, and logistic capabilities of the CDC and the Department of Health and Human Services (DHHS).

On March 24, scientists at the CDC and in Hong Kong announced that a new coronavirus had been isolated from patients with SARS. Over the next two weeks, the machinery to discover and characterize the pathogen was set in full motion by scientists at the CDC and in other WHO collaborating laboratories. Within days, sequences of the coronavirus polymerase gene were compared with those of previously characterized strains, and scientists were able to say with confidence that this virus was distinct from all known human pathogens. In addition, serum samples from patients with SARS were evaluated to detect antibodies to the new coronavirus, and seroconversion was documented in several patients with appropriate acute- and convalescent-phase specimens in laboratories at the CDC and elsewhere.

Coronavirus is now accepted by the scientific community as the cause of SARS. International laboratories have found evidence of coronavirus in patients with SARS, using a variety of methods including tissue culture, electron microscopy, microarray technology, indirect immunofluorescent antibody tests, and polymerase-chain-reaction amplification of specific genomic sequences. As of the end of April, assessment of the accuracy of potential diagnostic tests based on some of these methods has progressed to the point where new case definitions that include laboratory test criteria are under final review and production of test reagents for widespread distribution is well under way. In addition, laboratory testing of antiviral compounds that might be of therapeutic or prophylactic value is under way. Finally, initial steps toward vaccine development have already begun.

Even more impressive than the speed of scientific discovery in the global SARS outbreak is the almost instantaneous communication and information exchange that has supported every aspect of the response. The WHO, the CDC, and national and local health agencies across the globe have disseminated up-to-the-minute information tailored for clinicians, public health officials, health care workers, travelers, household contacts, and many other affected parties. Immediate communication of "interim" guidance, updated as soon as new information becomes available, has become the norm. Use of the Internet has sped information exchange and helped overcome the problems presented by asynchrony in the activities of investigators in many time zones. Scientists at the international collaborating laboratories are exchanging laboratory results and images on a secure Web site. Coordination of the international response strategy has been fostered by regular videoconferences with senior leaders in the operations centers at the WHO, the DHHS, and the CDC. Satellite broadcasts, Webcasts, and videoconferencing are supporting the dissemination of emerging information to the entire global health community. The international media have also played an around-the-clock part in communicating breaking news to the public by television, radio, print publications, and the Internet.

Speed of scientific discovery and speed of communication are hallmarks of the response to SARS and reflect amazing achievements in science, technology, and international collaboration. However, despite these advances, a very sobering question remains — are we fast enough? Can we prevent a global pandemic of SARS? The epidemic is progressing rapidly in many parts of Asia. The situation in mainland China is not entirely clear, but the available information strongly suggests that there is ongoing transmission in at least some provinces. The

epidemic is still expanding in Hong Kong, despite heroic measures on the part of the government to curtail its spread. Clusters of cases in community settings such as hotels and apartment buildings in Hong Kong demonstrate that transmission can be extremely efficient. Likewise, very high attack rates among health care workers in Hanoi, Vietnam, and in hospitals in Hong Kong document the highly contagious nature of this virus, at least in some circumstances. Many household contacts have become ill. Concern is mounting about the potential for spread in schools, the workplace, airplanes, and other crowded areas. New cases among travelers from affected areas continue to emerge and have led to infections in household contacts and health care personnel in many countries, including the United States and Canada.

The epidemic of SARS is apparently only months old, and it is entirely too soon to predict its ultimate scope or magnitude. Epidemiologic evidence indicates that the transmission of SARS is facilitated by face-to-face contact, and this still appears to be the most common mode of spread. Some evidence suggests that a few persons may be especially infectious and that most others are less likely to serve as sources of infection, but this concept is still speculative. Airborne transmission may have a role in some settings and could account for the extensive spread within buildings and other confined areas that has been observed in some places in Asia. Certainly, airborne transmission will make containment of the epidemic much more challenging. Fomite transmission could also be relevant, since coronaviruses can survive on contaminated objects in the environment for at least a few hours, and fecal–oral transmission has been proposed as a mode of transmission in some Hong Kong apartments. Despite our long experience with other viral respiratory infections, we have no proven, successful population-based strategy for their prevention. Even when we have an effective vaccine, as in the case of influenza, annual infection rates and attributable mortality remain very high. If SARS transmission evolves to mimic that of influenza, containment may well be impossible without vaccination, prophylaxis, or treatment.

There is reason to be optimistic about future control measures. Vaccines are successful in preventing coronavirus infection in animals, and the development of an effective vaccine against this new coronavirus is a realistic possibility. Likewise, novel antiviral agents, antiviral drugs in development, or existing licensed drugs could be found to provide effective prophylaxis or treatment. But can we make these products available fast enough to prevent an extensive global outbreak? Recent experience with the advances in measures against bioterrorism suggests that the pace of development can be dramatically accelerated. However, potential rate-limiting steps include the development of suitable animal models to demonstrate efficacy, the time necessary to demonstrate the safety of any new product in adults and children, and the time and resources needed to increase production to meet global market needs.

The emergence of SARS presents formidable global challenges. If we are extremely lucky, the epidemic will be curtailed, develop a seasonal pattern that will improve prospects for regional containment, or evolve more slowly than it has in this early stage. If the virus moves faster than our scientific, communications, and control capacities, we could be in for a long, difficult race. In either case, the race is on. The stakes are high. And the outcome cannot be predicted.

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